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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,370	05/21/2004	Shyh-Horng Chiou	4910-9DIV	2287

7590 03/28/2006

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EXAMINER

SWOPE, SHERIDAN

ART UNIT	PAPER NUMBER
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1656

DATE MAILED: 03/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/626,370

Applicant(s)

CHIOU, SHYH-HORNG

Examiner

Sheridan L. Swope

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8-13 is/are pending in the application.
- 4a) Of the above claim(s) 10-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8 and 9 is/are rejected.
- 7) ☒ Claim(s) 8 and 9 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>0703</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's election without traverse of Invention II, Claims 8-13, in their response of January 3, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 8-13 are pending. Claims 10-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 8 and 9 are hereby examined.

Priority

The priority date of the instant invention is taken to be August 24, 2001, the filing date of US 09/939,126.

Title

The title is objected to for being too long and not being descriptive of the elected invention.

Information Disclosure Statement

The Information Disclosure Statement of July 24, 2003 has been fully considered. However, reference AI and AK on page 3, AL and AM on page 4, AF and AG on page 5, and AG on page 6 are incomplete, missing either an author, year, volume, or page numbers. Applicants are requested to submit a supplemental Information Disclosure Statement providing the complete citation for the above references.

Specification-Objections

The specification is objected to for the following reasons.

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The specification at page 18, lines 2-8, page 20, line 16, and page 23, lines 1-2, discloses sequences that are not identified by a sequence identifier number (SEQ ID NO:). The sequence rules embrace all nucleotide sequences with ten or more bases and all amino acid sequences with four or more amino acids. Said sequences must be disclosed in a sequence listing and identified by a specific SEQ ID NO: (MPEP 2421.02). 37 CFR 1.821(d) requires the use of the assigned sequence identifier number in all instances where the description or claims of a patent application discuss sequences, regardless of whether a given sequence is also embedded in the text of the description or claims of an application. Applicant is required to correct the above pages to identify all of the sequences disclosed therein by sequence identifier numbers.

The specification is objected to for using the terms "Tm-5", "Tm-VIG", and "Tm-IIG" interchangeably. The term "Tm-5" is not defined by the specification. A person of ordinary skill in the art would not be apprised of the disclosed invention.

The specification is objected to for having large blank spaces on pages 6 and 9.

Claims-Objections

Claim 8 is objected to for the following reasons. On line 1, "proteases" should be "protease". On line 2, "autocatalytic" should be "autocatalytic". On line 2, "the cleavage sequence" lacks antecedent basis and should be "a cleavage sequence".

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 8 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

The phrase “A vector for expressing a protease...” renders Claim 8 indefinite. It is unclear whether said phrase is meant to mean “A protein expression vector comprising a sequence encoding a protease...” or “A vector capable of expressing a protease...”. The latter would encompass any vector capable of protein expression. Clarification is required. Claim 9, as dependent from Claim 8 is rejected for the same reason. For purposes of examination, it is assumed that the phrase “A vector for expressing a protease...” is meant to mean “A protein expression vector comprising a sequence encoding a protease...”.

The phrase “expression product” renders Claim 8 indefinite, as neither the specification nor the claims provide a definition for said phrase. It is unclear whether said phrase refers to a protein encoded by the recited vector or an expression product from another source. Clarification is required. Claim 9, as dependent from Claim 8 is rejected for the same reason. For purposes of examination, it is assumed that the phrase “expression product” refers to a protein encoded by the recited vector.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 8 and 9 are rejected under 35 U.S.C. 112, first paragraph. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 8 and 9 are so broad as to encompass any vector encoding any protease comprising the cleavage sequence of SEQ ID NO: 2, wherein the protease is capable of cleaving said cleavage sequence by an autocatalytic process. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of vectors encoding an extremely large number of proteases, as broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which polypeptides can cleave the peptide of SEQ ID NO: 2 requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any,

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are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function.

However, in this case the disclosure fails to provide the nucleic acid sequence encoding any polypeptide comprising the peptide of SEQ ID NO: 2 and capable of cleaving said peptide by an autocatalytic process. Moreover, the specification fails to provide any guidance on how any known polypeptide can be modified in order to obtain the desired ability to autocatalytically cleave the peptide of SEQ ID NO: 2.

While recombinant and mutagenesis techniques as well as protease assays are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims. Furthermore, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable (Galye et al, 1993; Whisstock et al, 2003). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of Claims 8 and 9 which, encompasses all vectors encoding any protease comprising the peptide of SEQ ID NO: 2, wherein the protease is capable of autocatalytically cleaving said peptide. The specification does not support the broad scope of Claims 8 and 9 because the specification fails to disclose: (A) any nucleic acid sequence encoding any polypeptide comprising the peptide of SEQ ID NO: 2, wherein the polypeptide is capable of autocatalytically cleaving said peptide; (B) regions of any protein's structure which may be modified to obtain the desired activity; (C) regions of any

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protein's structure which may be modified without effecting the desired activity; (D) the general tolerance of the desired activity to modification and extent of such tolerance; (E) a rational and predictable scheme for making any polynucleotide encoding a polypeptide having the desired activity; (F) a rational and predictable scheme for modifying any residues of any polynucleotide encoding any protein with an expectation of obtaining the desired biological function; and (G) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of vectors comprising any sequence encoding a protease comprising the peptide of SEQ ID NO: 2 and able to cleave said peptide by an autocatalytic process. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

Written Description

Claims 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules encoding any

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polypeptide comprising the peptide of SEQ ID NO: 2, wherein the polypeptide is a protease able to cleave said peptide by an autocatalytic process. The specification teaches the structure of no representative species of such DNAs. Moreover, the specification fails to describe any representative species by any identifying characteristics or properties other than the functionality of encoding a polypeptide comprising the peptide of SEQ ID NO: 2, wherein the polypeptide is a protease able to cleave said peptide by an autocatalytic process. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages. It is also requested that Applicants identify support, within the original application, for any amendments to the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.


Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application

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may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheridan Lee Swope, Ph.D.

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**SHERIDAN SWOPE, PH.D.
PRIMARY EXAMINER**